Reducing Uncertainty in the Evaluation of Stem Cell Colonies

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***Abstract*— Pluripotent cells are inherently unstable. Colonies of pluripotent cells differentiate, in whole, or in part into cell types with distinct morphological properties. Laboratories around the world make frequent quality-control decisions about passaging colonies based on their visible microscopic characteristics. To the observer, these characteristics indicate desirable properties such as pluripotency and viability. Thus, site-to-site variability and scientist-to-scientist variability can significantly contribute to variability in biological outcome and irreproducibility in conclusion. If mathematical descriptions of the relevant colony features could be developed, and appropriate classifiers could be designed to distinguish colonies based on quality, consistency would be assured, and automation of expansion and passaging of stem cells would be made possible. In this study, stem cell colonies were imaged with a standard 10x phase contrast objective using a defined protocol and a reference material to facilitate reproducible imaging conditions. The images (480 total) were examined by two experts and scored on a scale from 5 (for the best pluripotent colonies), to 1 (those with the least pluripotent character). A set of 96 image analysis derived features were evaluated to identify those most predictive of the expert scores. We found that a simple linear model containing three image analysis derived features performs as well as when the experts' scores are compared against one another. This quantitative description of a stem cell colony can be used to unambiguously select colonies and examine the reproducibility of a culture system or to compare these selection rules with putative antibody labels for pluripotency.**

***Index Terms*— stem cells, uncertainty of cell colony ranking**